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RESEARCH ARTICLE

Clinical scales in autoimmune encephalitis—A retrospective monocentric cohort study

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Abstract

Objective: Assessing severity of antibody-mediated encephalitis (AE) or paraneoplastic encephalitis (PE) requires valid and reliable scores to guide treatment decisions and predict outcome both in clinical routine and studies. We aimed to validate the prognostic value of the clinical assessment scale in autoimmune encephalitis (CASE) and the anti-NMDAR-encephalitis one-year functional status (NEOS) score in patients suffering from AE and PE in a large monocentric cohort. **Methods**: We retrospectively applied the CASE and NEOS score to patients with definite AE and PE treated at a tertiary hospital. Correlations were established between the CASE and NEOS score and the modified Rankin scale (mRs). Multivariable analyses were calculated to identify predictors of outcome. **Results**: Thirty-four patients (27 AE, 7 PE) were included. Correlations between mRS and CASE score were strongest in patients with AE compared to PE at all intervals, but in the subgroups (LGI1, NMDAR, GAD, miscellaneous surface antibodies, PE) the correlation was strongest in the interval after baseline. Patients with AE seemed to display better outcomes compared to PE, which was underlined by multivariable analysis. Improvement was mostly observed within 6–12 months after disease onset, after which little or no further improvement was noted with some exception for two patients with anti-NMDARE who recovered substantially even after 12 months of treatment. The NEOS score significantly predicted the outcome at last follow-up in patients with AE with a sensitivity of 79% at a cut-off value of 2 points (AUC 0.79, 95% CI 0.58–0.99, $p = 0.04$). **Interpretation**: The CASE and NEOS score are suitable supplementary tools in addition to the mRS for capturing diverse symptoms, for grading and monitoring symptom severity.

Introduction

Reflected by rising incidence rates, antibody-mediated encephalitis (AE) is increasingly recognized and, thus, antibody-specific syndromes have been well characterized.[1–6] Functional outcome in AE and paraneoplastic encephalitis (PE) is mainly assessed using the modified Rankin scale (mRS), a 7-point scale originally designed to evaluate and predict outcome in stroke patients.[7,8]

Although the mRS indicates significant clinical changes, it is severely limited in terms of interrater reliability and also fails to capture functional deficits in patients with AE or PE, such as cognitive abilities.

The prerequisite for assessing treatment effects are clinical assessment scores that are easy to use and that capture the relevant domains impacted by AEs and PEs. Therefore, the clinical assessment scale in autoimmune encephalitis (CASE) and the anti-NMDAR encephalitis one-year functional status (NEOS) score were developed to grade disease severity in patients suffering from AE and to estimate disease severity based on current data in patients with anti-NMDARE, respectively.

The objective of the present study was to assess the CASE and NEOS scores as prognostic measures in a monocentric cohort of AE and PE patients.

Material and Methods

Ethics

This study was approved by the ethics committee at the Medical University of Vienna (EK 1773/2016; 1123/2015).

Study population

Thirty-four patients from the Department of Neurology, Medical University of Vienna, and with a confirmed diagnosis of AE or PE between 2014 and 2020 were retrospectively reviewed. All patients fulfilled the Graus criteria for AE 2016 or PE from 2021,[9] respectively.[10] Patients with a follow-up interval of at least 12 months were included. We defined the "last follow up" timing as the last physical examination prior to study inclusion. We excluded patients with alternative diagnoses, including infectious encephalitis (e.g., confirmed by viral detection by medium PCR in cerebrospinal fluid [CSF]).[10] Autoantibodies were determined using an in-house tissue-based assay and a commercial cell-based assay (Euroimmun) as reported elsewhere.[7] Patients were divided into an AE and a PE cohort. The AE group was further subdivided according to antibodies to (1) NMDAR, (2) LGI1, (3) GAD65/67, and (4) miscellaneous surface antibodies including two CASPR2, one AMPAR, two glycine receptor, and three IgLON5.

Scores

The NEOS score and the CASE score were retrospectively applied to our cohort of patients with AE at the time of admission and over the follow-up period in 6 months intervals. The CASE is a 9-item scale with a total score maximum of 27 points proposed to assess severity in patients with diverse AE syndromes.[11] The NEOS score consists of five items and was shown to predict the 1-year functional outcome in patients with anti-NMDARE. A high score indicates worse clinical status or prognosis, respectively. Good recovery was defined as a mRS score of 0–2 points.

Statistical analysis

Statistical analysis was performed using SPSS 26.0 (SPSS Inc, Chicago, IL, USA). Descriptive statistics were used for demographic and clinical data. Categorical variables were expressed in frequencies and percentages, and nonparametric variables as median and range. Normal distribution was assessed by Kolmogorov–Smirnov. Univariate correlations between CASE, mRS and NEOS scores were analyzed by Pearson or Spearman test as appropriate. Primary focus was put on assessments at the timepoints: baseline, after 1 year, and at last follow-up. In addition, the development of CASE and mRS scores in the overall cohort and in the subgroups of AE, PE, and various antibodies was presented over time. We performed receiver operating characteristic (ROC) analyses to determine the best cut-off values for CASE and NEOS in order to discriminate between patients with good (mRS 0–2) and unfavorable (mRS 3–6) outcome. Multivariable binary logistic regression models were run to examine the results, with the mRS score at 1 year and at the last follow-up as dependent variables and age, sex, the CASE score at baseline, the NEOS score, and group assignment (reference category: PE) as independent variables. A Kaplan–Meier curve was created to illustrate the time to achieve a good result (mRS 0–2) in the different subgroups. A two-sided p-value <0.05 was considered statistically significant.

Results

Twenty-seven patients with AE (Twenty-one with antibodies against surface epitopes, six with anti-GAD antibodies) and seven patients with antibodies against intracellular epitopes met the inclusion criteria (see Table 1). The AE cohort consisted of seven anti-LGI1 patients of which six presented with limbic encephalitis (LE) and one with neuromyotonia. All six patients with anti-GAD antibodies suffered from stiff person spectrum disorder (SPSD) and/or limbic encephalitis. The six patients with anti-NMDARE had a stereotype disease course requiring intensive care support. Further, two patients with anti-GlyR antibody-mediated SPSD, two patients with anti-CASPR2 antibody-mediated LE, three patients with anti-IgLON5 disease (one LE, two predominantly brainstem symptoms), and one patient with anti-AMPAR antibody-mediated LE have been included in the miscellaneous surface antigen group. Patients with PE presented with a cerebellar and/or brainstem syndrome (five out of six) or limbic encephalitis (one out of six) (for patient details, see Table 1).

Patients with anti-NMDARE scored highest on the mRS scale (median mRS 5, median CASE 18.5) and CASE scores at baseline yet exhibited the highest dynamics in terms of outcome scores and clinical recovery at follow-up. Similarly, 6 out of 7 patients with anti-LGI1 limbic encephalitis showed good recovery at last follow-up, which is also partly applicable to patients with other neuronal surface antibodies (8 out of 14). Patients with PE and GAD65/67 encephalitis were clinically severely affected at baseline and showed little dynamic over the

Table 1. Baseline characteristics at time of admission.

	AE (n = 27)	PE (n = 7)
Age (years) Median, min.–max.	58 (22–80)	61 (53–76)
Sex (female)	17 (63.0)	6 (85.7)
Follow-up (years) Median, min.–max.	2 (1–5.5)	2 (1–3)
Antibodies (serum and/or CSF)	LGI1 n = 7 GAD n = 6 NMDAR n = 6 Miscellaneous surface: Glycine n = 2 CASPR2 n = 2 IgLON5 n = 3 AMPAR n = 1	Yo n = 4 CV2 n = 1 Ma2 n = 2
EEG abnormalities*,#	LGI1 3/7 GAD 1/3 NMDAR 6/6 Misc. surface 5/6	Ma2 1/1
cMRI abnormalities**	LGI 1 7/7 GAD 3/6 NMDAR 1/6 Surface 5/8	Yo 0/4 CV2 0/1 Ma2 1/2
CSF abnormalities***	LGI1 2/7 GAD 5/6 NMDAR 6/6 Misc. surface 3/7	Yo 4/4 CV2 1/1 Ma2 1/2

CASPR2, contactin-associated protein-2; cMRI, cranial magnetic resonance imaging; CSF, cerebrospinal fluid; EEG, electroencephalogram; GAD, glutamic acid decarboxylase; Glycine, glycine receptor; LGI1, leucine-rich glioma inactivated 1 protein; NMDAR, N-methyl-D-aspartate receptor.

*Focal or diffuse slow or abnormal activity, epileptic activity, or extreme delta brush.

**MRI suggestive of encephalitis according to Graus et al.[10]

***White blood cell count >5 c/μL, intrathecal IgG or ≥2 oligoclonal bands.

#EEG was only conducted if an epileptic seizure was clinically suspected.

observation period. None of our patients with PE achieved a good outcome (mRS Score 0–2) at last follow-up (see Table 2). Remarkably, clinical improvement was greatest within the first 12 months after admission (see Fig. 1), although two patients with NMDARE and ICU treatment also showed a significant response to immunotherapy far beyond 12 moths of disease course.

Correlations between mRS, CASE and NEOS scores

Overall cohort

Relative to the entire study population, the CASE score correlated strongly with the corresponding mRS score at baseline, 1 year, and at the last follow-up, with a weaker correlation at baseline than at subsequent time points ((baseline: $r = 0.68$, $p < 0.01$; 1 year: $r = 0.79$, $p < 0.01$; and last follow-up: $r = 0.84$, $p < 0.01$; see Fig. S1). The NEOS score correlated moderately with the CASE score at last follow-up ($r = 0.38$, $p = 0.04$) and the mRS after 1 year ($r = 0.39$, $p = 0.02$).

Subgroup analysis

The CASE score at baseline, after 1 year and at last follow-up correlated strongly with the corresponding mRS score (baseline $r = 0.56$, $p \leq 0.01$; 1-year $r = 0.82$, $p \leq 0.01$; last follow-up $r = 0.83$, $p \leq 0.01$) in the whole study cohort. This was also applicable for the AE subgroup (baseline $r = 0.68$, $p \leq 0.01$; 1 year $r = 0.79$, $p \leq 0.01$; last follow-up $r = 0.84$, $p \leq 0.01$). Besides from the miscellaneous surface group the CASE score at baseline did not correlate significantly with the corresponding mRS score in the LGI1, NMDAR, and GAD subgroup but turned significant after 1 year and at last follow-up in the LGI1, NMDAR, and miscellaneous surface group. In consequence this indicates that the CASE score did not correlate well with the mRS score at clinical nadir but only after recovery (see Table S1).

The NEOS score correlated significantly with the 1 year mRS score in the NMDAR group ($r = 0.88$, $p = 0.02$), the miscellaneous surface group ($r = 0.72$, $p \leq 0.01$) and the AE group ($r = 047$, $p = 0.03$) when excluding antibodies

Table 2. Subgroup characteristics.

		Baseline scores			1 year		Last follow-up	
Group	n	mRS[1]	CASE[1]	NEOS[1]	mRS[1]	CASE[1]	mRS[1]	CASE[1]
LGI1	7	3 (2–3)	5 (4–8)	3 (1–4)	1 (0–2)	2 (0–4)	1 (0–3)	1 (0–5)
GAD65/67	6	3.5 (2–4)	4 (2–7)	2 (1–3)	4 (2–4)	3 (2–5)	4 (2–4)	3 (2–6)
NMDAR	6	5 (5)	18.5 (12–25)	2 (2–5)	1 (0–5)	2.5 (0–17)	0.5 (0–4)	0.5 (0–6)
Surface	8	3 (2–5)	4.5 (2–15)	2 (1–4)	3 (0–6)	3 (0–5)	3 (0–6)	2.5 (0–4)
PE	7	4 (4)	4.5 (2–7)	2.5 (2–3)	4 (4–6)	5 (3–7)	4 (4–6)	5 (3–7)

GAD, glutamic acid decarboxylase; LGI1, leucine-rich glioma inactivated 1 protein; NMDAR, N-methyl-D-aspartate receptor; PE, paraneoplastic encephalitis; Surface, antineuronal surface antibodies.

[1]Median (min.–max.).

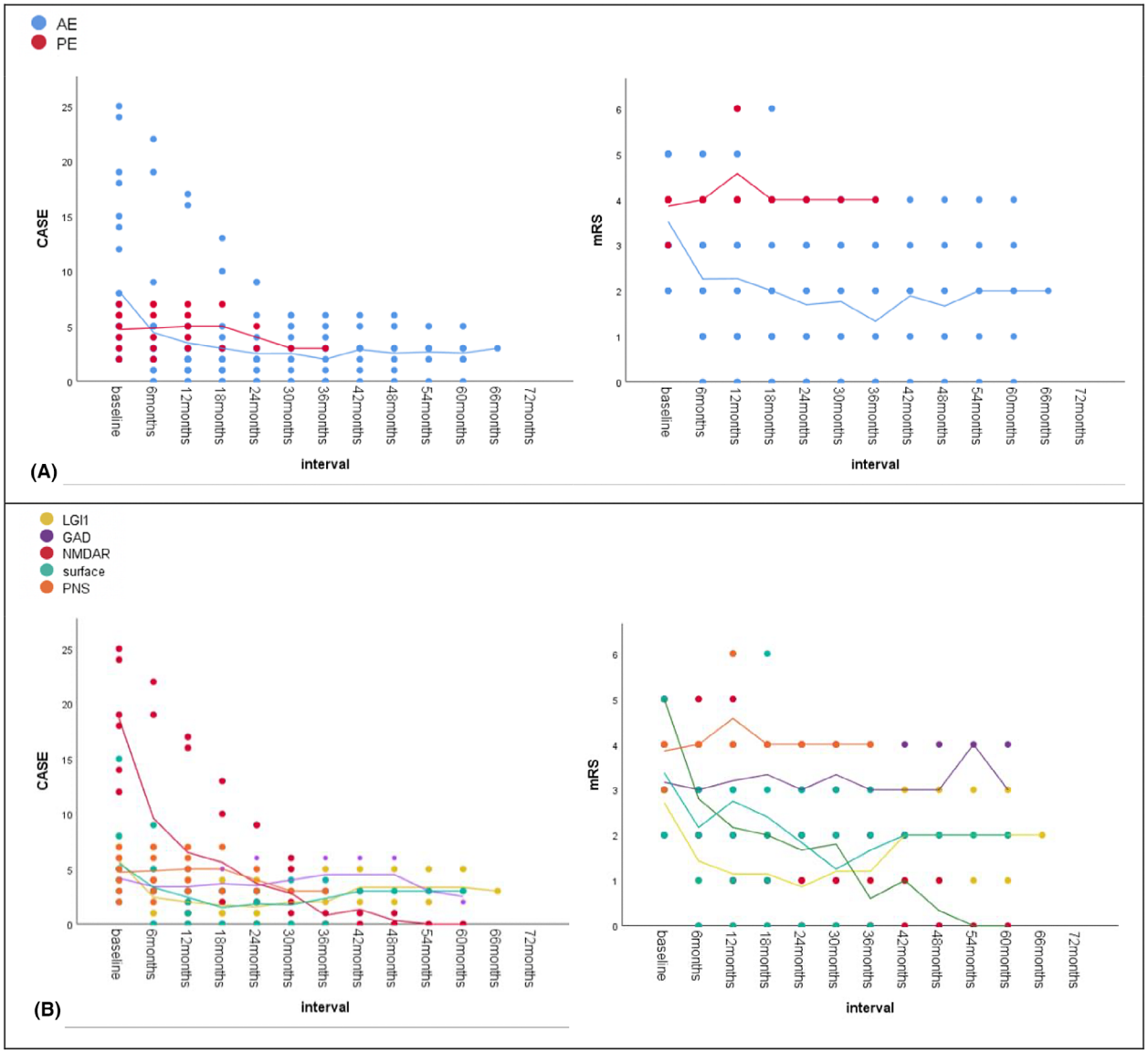

Figure 1. Illustrates the distribution of mRS and CASE scores in our total population with AE and PE (A) and in different subgroups (B). The colored lines represent the mean value of the course in the respective groups. A: Both scores show the most impressive improvement within the first 12 months after diagnosis in patients with AE whereas patients with PE show a stable course; the CASE score is higher in patients with AE compared to PE at baseline indicating that the CASE captures a greater variety of symptoms and better depicts the clinical picture of patients with AE. B: The CASE score rather than the mRS score better illustrates the bandwidth of symptoms present and forthcoming improvement especially in patients with anti-NMDARE followed by anti-LGI1 and other surface abs compared to patients with anti-GAD syndromes and paraneoplastic encephalitis.

directed against intracellular epitopes (GAD, PE) but not with the 1 year CASE score. No significant correlations of the NEOS score with the 1 year follow-up mRS score was observed in the AE, PE, LGI1, and GAD group.

Predictive factors of outcome

A multivariable analysis applied to the entire study population using a binary 1-year mRS score (0–2 points and 3–6 points for good and poor recovery, respectively) revealed group affiliation to PE (with reference to AE) to be a significant predictor of worse outcome at 1 year, and a high NEOS score and PE to be significant predictors of worse outcome at last follow-up (see Table 3).

ROC results

In the overall cohort the NEOS score was a significant predictor of poor outcome at last follow-up but not after 1 year. Still a NEOS score of ≥2 only had a sensitivity of

Table 3. Factors associated with outcome; binary logistic regression model (overall cohort R^2 0.65, $p < 0.01$, respectively) reference mRS 3–6.

	Overall 1-year mRS		Overall last FU mRS	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Age	1.09 (1.0–1.20)	0.06	1.09 (0.99–1.19)	0.09
Male sex	0.15 (0.01–2.02)	0.15	0.70 (0.07–7.40)	0.77
NEOS score	3.63 (0.84–15.75)	0.09	5.67 (1.24–25.96)	0.03*
CASE baseline	1.17 (0.91–1.51)	0.22	0.99 (0.77–1.25)	0.90
PE[1]	0.03 (0.01–0.50)	0.02*	0.04 (0.01–0.66)	0.03*

AE, antibody-mediated encephalitis; FU, follow-up; PE, paraneoplastic encephalitis.
[1]Reference category: AE.
*Significant.

69% with a false-positive rate 47% to discriminate between good and poor outcome at last follow-up (AUC 0.69, 95% CI 0.50–0.87, $p = 0.07$) in our total cohort and a sensitivity of 69% with a false-positive rate of 50% in patients with AE (AUC 0.69, 95% CI 0.48–0.90, $p = 0.11$). When excluding patients with PE and GAD antibodies from the model a NEOS score of ≥2 had a sensitivity of 71% with a false-positive rate of 29% (AUC 0.79, 95% CI 0.58–1.0, $p = 0.04$).

Final outcome

The clinical course of patients with antibodies targeting neuronal surface proteins was less severe compared to patients with anti-GAD antibodies or PE. None of the PE cohort patients did have a good outcome as documented by mRS 0–2. The most marked clinical improvement was noted within the first year after initiation of therapy.

Discussion

We applied the CASE and the NEOS score on our cohort of patients suffering from definite AE and PE and used the mRS as reference rating tool. The CASE is a 9-item scale with a total score maximum of 27 points proposed to assess severity in patients with diverse AE syndromes.[11] The scale was developed and validated in a two-cohort approach with 88 patients suffering from AE. For validation, both direct examination and retrospective review of medical records were performed. The NEOS score consists of five items and was shown to predict the 1-year functional outcome well when applied to a cohort of 382 patients suffering from anti-NMDARE. The mRS score is widely used as it can easily be performed, and gives reliable information on the patient's global functional status. A high score in each of the investigated scales (mRS, CASE, NEOS) indicates a worse outcome. The choice of scales is limited, and both the clinical utility and prognostic therapeutic value of the known instruments were tested in relatively small cohorts due to the rarity of the diseases. Assessment scales of cognitive and functional recovery in patients with AE are needed to assess reliable outcome and make it comparable to study therapeutic interventions, moreover the use of specific rating scales may overcome the pluralism of combining different scales.

In the overall cohort of patients with AE and in the majority of our patients with anti-NMDARE, anti-LGI1 encephalitis, and partially in patients with other surface antibodies, we observed good recovery (mRS 0–2) over time, while patients in the anti-GAD and PE cohort showed little or no clinical improvement. Recovery occurred in most patients within the first 6 months after onset and was most evident in patients who had anti-NMDARE, followed by patients in the LGI1 group and the miscellaneous surface group. Noteworthy patients with NMDAR, AMPAR, LGI1, or CASPR2 antibodies showed a less severe disease course than patients with anti-IgLON5 or anti-glycine receptor antibodies which accounts for the biphasic course of the miscellaneous surface group after initial improvement (see Fig. 1 and Fig. S2). Patients with anti-GAD antibodies, though non-paraneoplastic, showed a similar course compared to patients in the PE group and only exhibited minor response to immunotherapy. Although most patients in the AE groups showed only little improvement after 6 months, in two patients with anti-NMDARE clinical improvement was noted far beyond the 12 months threshold indicating that it is important to continue immunotherapy also in later stages. It was also noticeable that patients in the anti-NMDARE group were significantly younger (median 27 years, min.–max. 22–44 years) than patients from other subgroups ($p = 0.03$).

The use of the CASE score allows a more detailed recording of symptoms than when using the mRS score. In our cohort this refers to patients that usually have a relatively high score on the mRS and a relatively low score on the CASE especially at baseline rating. Our results are not necessarily in line with findings of other studies who reported that the CASE score correlated better with mRS results when patients were in a worse clinical condition.[12–17] In the AE group, both scales correlated at baseline ($r = 0.68$, $p \leq 0.01$), this was also true after 1 year (1 year $r = 0.79$, $p \leq 0.01$), and at last follow-up ($r = 0.84$, $p \leq 0.01$) when recovery was observed in most patients. Similar results were observed when applying the scale on the overall cohort. Scores at baseline showed only weak and nonsignificant correlations in the subgroups except for the miscellaneous surface group. In the

subgroups, besides the small sample sizes, symptom severity depending on the antibody present and different sensitivities of the mRS and CASE score in capturing patients' symptoms might explain only poor and nonsignificant correlations at baseline.

In our NMDAR cohort a higher CASE score at baseline was associated with a higher score after 1 year ($r = 0.88$, $p = 0.02$) and at last follow-up ($r = 0.94$, $p \leq 0.01$) which was also true when applying mRS scores to the miscellaneous surface group (1 year: $r = 0.80$, $p = 0.02$; last follow-up: $r = 0.76$, $p = 0.03$). One could assume that a bad clinical condition at admission is indicative of a worse clinical outcome (see Fig. 1 and Table S1).

In our cohort the NEOS score correlated best with the mRS score after 1 year in the NMDAR group ($r = 0.88$, $p = 0.02$) followed by the miscellaneous surface group ($r = 0.72$, $p < 0.01$) and AE ($r = 047$, $p = 0.03$) excluding patients with anti-GAD syndromes and PE. The best cut-off was observed in our cohort with AE excluding patients with anti-GAD antibodies and the PE group; a score ≥2 had a sensitivity of 71% with a false positive rate of 29% (AUC 0.79, 95% CI 0.58–1.0, $p = 0.04$).

We recognized several caveats when conducting the CASE score. First, the CASE score could reflect the clinical course well but it might have some weaknesses in rating brainstem and cerebellar symptom severity and progression. Patients scoring low in the CASE score should not automatically be categorized in having low symptom severity as shown in our subgroup analysis. As emphasized previously an isolated gait disturbance may score 2 out of 27 points in the CASE but 4 out of 6 points in the mRS score. The mRS score spares information on the remaining functional and cognitive status. The CASE score, on the other hand provides additional information on strength deficits, dyskinesias, and brainstem symptoms in gait disorders. Second, some categories in the CASE score are left open regarding implementation and were not precisely defined in the original publication. For example the timing of the score might have a major impact on the results.[16] We noticed great discrepancies between the CASE score and mRS score in patients with stiff person spectrum disorder presenting with gait instability and task-specific phobia. While those patients' ambulation ability is often severely restricted, it was only reflected on the gait instability/ataxia item or even in the dyskinesia/dystonia item accounting for a maximum of 6 out of 27 points. The ability to walk, a major aspect in being independent in daily activities, is heavily weighted on the mRS score. This implicates that a low score on CASE scale does not permit to infer a minor impact on everyday life as is the case, for example, with the mRS or the National Institute of Health Stroke Scale. One anti-IgLON5 patient exhibited a unilateral vocal cord palsy which soon evolved bilaterally. Tube feeding was not necessary, and the patient suffered from dysphonia but was able to express full sentences and therefore only received 1 point in the CASE score and 2 points in mRS score. The authors argue that the 9-item of the CASE Score incorporates a variety of symptoms occurring in autoimmune encephalitis other than the mRS score, which mainly focuses on motor symptoms. This addresses the problem that patients might be in severe neuropsychiatric state but may be able to walk unassisted, thus scoring low on the mRS scale.

The validity of our results is limited by the small study population, thus it is difficult to draw general conclusions. However, our patients with antineuronal surface AE tended to have better clinical outcomes than PE when treated early and appropriately. The effect of immunotherapy on clinical outcomes in classic PE is highly controversial as randomized controlled trials are missing, patients generally receive immunotherapy as add-on treatment and only small sample size studies report on outcome of PE. Stabilization or minimal improvement was reported in 50% of patients with PE and high-risk antibodies 6 months after being treated with immunotherapy and in 1 out of 17 patients with anti-Hu-associated syndromes.[12–14] This is in contrast to anti-NMDARE in which tumor resection, independent of tumor etiology, is an important treatment-factor, resulting in good outcome (mRS 0–2) in 81% after 24 months observation period.[3] However, in our population of PE (4 anti-Yo, 2 anti-Ma2, 1 CV2/CRMP5) all patients experienced tumor surgery. All patients with gynecological tumors and anti-Yo antibodies (1/4 N. mammae, 3/4 N. ovarii) and two patients with small-cell lung cancer (SCLC) and non-small-cell lung cancer (1 Ma2, 1 CV2/CRMP5), respectively, received chemotherapy and two patients had radiation therapy (1 Mamma Ca, 1 SCLC). All patients with anti-Yo syndrome received immunotherapy (first-line treatment in one-fourth and first- and second-line treatment in three-fourths of patients), two patients received first-line treatment (1 Ma2, 1 CV2/CRMP5) and a single patient with anti-Ma2 syndrome did not receive any immunotherapy. From our observations immunotherapy had no significant effects on clinical parameters in PE, still the underlying malignancy substantially influenced clinical outcomes. Patients with PE had a severe course without significant clinical improvement, similar was the course of our patients with GAD and IgLON5 antibodies.

The major limitation of our study is the retrospective design and the small study population ($n = 34$) which was further divided into several subgroups. The CASE and NEOS scores were applied retrospectively in this study certain symptoms might have been missed as not adequately documented in medical charts. Pooling anti-

CASPR2 and anti-AMPAR patients with mostly rather favorable clinical courses and patients with anti-IgLON5 and anti-glycine receptor antibodies with rather poor courses into the same group distorted the outcome of individual patients (see Fig. S2). The median mRS at last follow-up was 3p in the CASPR2 (0–6), 4p in the IglON5 (2–6), and 2p in the GlyR group (2,2). One patient with AMPAR receptor antibodies showed full recovery within 3 years of observation. Patients with anti-NMDARE were younger and hence had fewer comorbidities than patients in the other subgroups. Preexisting comorbidities but also sequelae from encephalitis (e.g., cognitive deficits, epileptic seizures, depression) and side effects of immunotherapy (neuropathy) might have influenced scoring. The observation intervals within the subgroups were heterogeneous (median/range): 3 years (2–5.5 years) in the anti-LGI1 group, 1.75 years (1–5 years) in the anti-GAD group, 3.25 years (2.5–4.5 years) in the anti-NMDAR group, 1 year in the PE group (1–3 years), and 2 years (1–5 years) in the surface group. However, we observed the most significant clinical improvement within the first 12 months after baseline (see Fig. 1). We believe, especially in the PE group in which all patients received tumor treatment (and 6 out of 7 received immunotherapy) but also in other subgroups with surface antigens, except GAD, a further improvement despite immunotherapy after 12 months would not be expectable.

The NEOS score was validated by the use of the mRS score and strongly predicted good or poor functional outcome after 1 year in patients with anti-NMDARE.[18,19] There was an attempt to adapt the NEOS score in a pediatric population which did not result in increased predictive power by the modified score. Still a higher score was a good predictor of poor clinical status after 1 year which was confirmed by another study in a pediatric cohort.[20,21] A modified variant of the NEOS score was validated and published in 2021.[22] The rationale was that clinical improvement within 4 weeks was not sufficiently defined. In this context, we defined any decrease in the mRS score compared with baseline findings as clinically relevant improvement and applied the original Score on our population.

We conclude that the more benign course of patients with antineuronal surface antibodies compared to patients with PE and anti-GAD antibodies can be depicted well with the CASE score. Especially in patients with anti-NMDARE with usually a diverse complex of symptoms, the CASE score is a useful assessment tool to capture the whole picture and for grading symptom severity and progression. It correlates well with the mRS score in our cohort of patients with AE and may be a suitable alternative or supplement to the mRS score as it is superior to the latter in monitoring symptom diversity, although it is not as easy to apply. The CASE score may not adequately capture the severity of comatose patients, and rules for the application of the score are ill-defined, leading to uncertainties. Further patients severely affected scoring relatively low in the CASE score might lead to an underrating of sequelae in patient reports, especially in case of investigators not being trained using the tool.

Author Contributions

Stefan Macher: conceptualization, methodology, formal analysis and investigation, writing. Gabriel Bsteh: methodology, formal analysis and investigation, supervision. Romana Höftberger: formal analysis and investigation, supervision. Thomas Berger: formal analysis and investigation, supervision. Paulus Rommer: conceptualization, methodology, supervision. Tobias Zrzavy: conceptualization, methodology, supervision.

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None.

Conflict of Interest

The authors declare no potential conflict of interest with any commercial entities relating to this study.

Data Availability Statement

Anonymized data, not published in the article, can be made available upon reasonable request from a qualified investigator after approval from the ethics review board of the Medical University of Vienna.

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1.
Figure S2.
Table S1.
Figure Captions.

